-37-

## **CLAIMS**

## 1. A compound of Formula I

$$\begin{array}{c|c} & & & \\ R^1 - \underset{H}{\overset{N}{\longrightarrow}} & \underset{O}{\overset{N}{\longrightarrow}} - so_2 - R^2 \end{array}$$

wherein R1 is

$$R^{3}$$
 $(A)_{m}$ 
 $R^{4}$ 
 $(A)_{m}$ 
 $(A)_{m}$ 

R<sup>3</sup> is hydrogen,

C<sub>1</sub>-C<sub>6</sub> alkyl,

 $-(CH_2)_n$  aryl, or

 $-(CH_2)_n$  heteroaryl;

10  $R^4$  is  $C_1$ - $C_6$  alkyl,

-( $CH_2$ )<sub>n</sub> aryl, or

- $(CH_2)_n$  heteroaryl;

 ${\rm R}^5$  and  ${\rm R}^6$  are each independently hydrogen,

C<sub>1</sub>-C<sub>6</sub> alkyl,

15  $-(CH_2)_n$  aryl, or

10

15

-(CH<sub>2</sub>)<sub>n</sub> heteroaryl;

 $R^7$  is  $C_1$ - $C_6$  alkyl,

-(CH<sub>2</sub>)<sub>n</sub> aryl, or

-(CH<sub>2</sub>)<sub>n</sub> heteroaryl;

each n is independently 0 to 6;

each m is independently 0, 1, 2, or 3;

A is alanine, leucine, isoleucine, proline, phenylalanine, glycine, tyrosine, serine, threonine, tryptophan, cysteine, methionine, valine, asparagine, glutamine, aspartic acid, lysine, glutamic acid, arginine, or histidine;

each RQ is independently hydrogen or C1-C6 alkyl;

 $R^2$  is  $-(CH_2)_n$ -Z; and

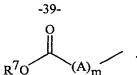
Z is aryl, heteroaryl, cycloalkyl, 
$$C_1$$
- $C_6$ alkyl,  $O$ 

$$\begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} \begin{array}{c} (\operatorname{CH}_2)_n \\ \end{array} \end{array} \end{array} \end{array} \\ \begin{array}{c} \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \end{array} \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \end{array} \end{array} \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \end{array} \end{array} \\ \begin{array}{c} \begin{array}{c} \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \end{array} \\ \begin{array}{c} \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \end{array} \end{array} \\ \begin{array}{c} \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \end{array} \end{array} \\ \begin{array}{c} \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \end{array} \\ \end{array} \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \\ \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array} \\ \begin{array}{c} \left(\operatorname{CH}_2\right)_n \\ \end{array}$$

$$C \longrightarrow (CH_2)_n$$
, fluorenyl, substituted fluorenyl, substituted  $(CH_2)_n$ 

aryl, substituted heteroaryl, or substituted cycloalkyl, and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

2. A compound according to Claim 1 wherein R<sup>1</sup> is



3. A compound according to Claim 1 wherein R<sup>1</sup> is

$$R^{7}O$$
 $(A)_{m}$ 

m is 0, and  $\mathbb{R}^7$  is  $-(\mathbb{C}H_2)_n$  aryl.

A compound according to Claim 1 wherein R1 is 5

m is 0, and  $R^7$  is -CH<sub>2</sub> aryl.

- A compound according to Claim 1 wherein R<sup>2</sup> is -(CH<sub>2</sub>)<sub>n</sub> aryl. 5.
- A compound according to Claim 5 wherein aryl is phenyl or naphthyl. 6.
- A compound according to Claim 1 wherein R<sup>2</sup>is -(CH<sub>2</sub>)<sub>n</sub> -cycloalkyl. 10 7.
  - A compound according to Claim 1 wherein R<sup>1</sup> 8.

$$O$$
  $O$   $(CH_2)_n$  phenyl or  $-SO_2$ -phenyl.

A compound according to Claim 1 wherein  $\mathbb{R}^2$  is 9.

10

10. A compound according to Claim 1 wherein R<sup>2</sup> is CH<sub>3</sub>

CH<sub>3</sub>

CH<sub>3</sub>

## 11. A compound of the Formula I

$$R^{1} - N \longrightarrow N - SO_{2} - R^{2}$$

wherein  $R^2$  is -CH<sub>2</sub>CH<sub>2</sub>- aryl, -CH<sub>2</sub>- cycloalkyl, -CH<sub>2</sub>CH<sub>2</sub>- cycloalkyl, or -CH<sub>2</sub>CH<sub>2</sub>- heteroaryl;

R1 is

$$R^{a}$$
,  $R^{b}$ ,  $R^{e}$ ,  $R^{e}$ ,  $R^{c}$ ,  $R^{d}$ ,  $R$ 

 $R^a$  is -(CH<sub>2</sub>)<sub>n</sub>- aryl or -(CH<sub>2</sub>)<sub>n</sub> heteroaryl;

Rb is aryl or heteroaryl;

Rc is -CH2 aryl or aryl;

Rd is hydrogen or C1-C6 alkyl;

R<sup>e</sup> is -CH<sub>2</sub> aryl or -CH<sub>2</sub> heteroaryl; and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

12. A compound according to Claim 11 wherein R<sup>1</sup> is



13. A compound according to Claim 11 wherein R<sup>1</sup> is

- 5 14. A compound according to Claim 11 wherein Re is -(CH<sub>2</sub>)<sub>n</sub> aryl.
  - 15. A compound according to Claim 14 wherein aryl is phenyl or naphthyl.
  - 16. A compound according to Claim 13 wherein Rb is aryl.
  - 17. A compound according to Claim 16 wherein is aryl is phenyl.
  - 18. The compounds:
- 10 3-Benzyloxycarbonylamino-4-oxo-5-(2-phenylethanesulfonylamino)-pentanoic acid;
  - 3-Benzyloxycarbonylamino-4-oxo-5-(3-phenyl-propane-1-sulfonylamino)-pentanoic acid;
  - 3-Benzyloxycarbonylamino-4-oxo-5-phenylmethanesulfonylamino-pentanoic acid;
  - 5-Benzenesulfonylamino-3-benzyloxycarbonylamino-4-oxopentanoic acid;
  - 3-Benzyloxycarbonylamino-5-methanesulfonylamino-4-oxopentanoic acid;
- 20 3-Benzyloxycarbonylamino-5-(naphthalene-1-sulfonylamino)-4-oxo-pentanoic acid;

		3-Benzyloxycarbonylamino-5-(2-cyclohexyl-ethanesulfonylamino)-
		4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(2-naphthalen-1-yl-
		ethanesulfonylamino)-4-oxo-pentanoic acid;
5		3-Benzyloxycarbonylamino-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(R)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(indan-1-ylmethanesulfonylamino)-
		4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(9-fluoro-9H-fluoren-9-
10		ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-Benzyloxycarbonylamino-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(S)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-(2-Acetylamino-3-methyl-butyrylamino)-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(S)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
15		3-(2-Acetylamino-propylamino)-5-(7,7-dimethyl-2-oxo-
		bicyclo[2.2.1]hept-1-(S)-ylmethanesulfonylamino)-4-oxo-pentanoic acid;
		3-(1,2,3,4-tetrahydro-1-oxo-isoquinoline-2-yl)-acetanino-
		5-benzenesulfonylamino-4-oxo-pentanoic acid;
		(S)-5-(Bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-3-[2-
20		(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-acetylamino]-pentanoic acid;
		(S)- 4-Oxo-3-[2-(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-
		acetylamino]-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid; and
		4-Oxo-3-[2-(1-oxo-3,4-dihydro-1H-isoquinolin-2-yl)-acetylamino]-
		5-phenylmethanesulfonylamino-pentanoic acid.
25	19.	A method of inhibiting interleukin-1ß converting enzyme, the method

comprising administering to a patient in need of inhibition of

compound of Claim 1.

interleukin- $1\beta$  converting enzyme a therapeutically effective amount of a

- 20. A method of inhibiting Caspase-4, the method comprising administering to a patient in need of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 1.
- 21. A method of treating or preventing stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 1.
  - 22. A method of treating inflammatory diseases, the method comprising administering to a patient having an inflammatory disease a therapeutically effective amount of a compound of Claim 1.
- 10 23. The method of Claim 22 wherein the inflammatory disease is arthritis.
  - 24. The method of Claim 22 wherein the inflammatory disease inflammatory bowel disease.
  - 25. A pharmaceutically acceptable composition that contains a compound of Claim 1.
- 15 26. A method of inhibiting interleukin-1β converting enzyme, the method comprising administering to a patient in need of inhibition of interleukin-1β converting enzyme a therapeutically effective amount of a compound of Claim 11.
- A method of inhibiting Caspase-4, the method comprising administering to a patient in need of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 11.
  - 28. A method of treating or preventing stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 11.

- 29. A method of treating inflammatory diseases, the method comprising administering to a patient having an inflammatory disease a therapeutically effective amount of a compound of Claim 11.
- 30. The method of Claim 29 wherein the inflammatory disease is arthritis.
- 5 31. The method of Claim 29 wherein the inflammatory disease is inflammatory bowel disease.
  - 32. A pharmaceutically acceptable composition that contains a compound of Claim 11.
- 33. A method of treating septic shock, the method comprising administering to a patient having septic shock a therapeutically effective amount of a compound of Claim 1.
  - 34. A method of treating septic shock, the method comprising administering to a patient having septic shock a therapeutically effective amount of a compound of Claim 11.
- 15 35. A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 1.
  - 36. A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 11.
    - 37. A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 1.

- 38. A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 11.
- 39. A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 1.
  - 40. A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 11.
- 10 41. A compound of the Formula II

wherein

R<sup>1</sup> is

$$R^{a}$$
,  $R^{b}$ ,  $R^{e}$ ,  $R^{e}$ ,  $R^{c}$ ,  $R^{c}$ ,  $R^{c}$ ,  $R^{c}$ ,  $R^{c}$ ,  $R^{d}$ ,  $R^{c}$ ,  $R^{d}$ ,  $R$ 

15  $R^a$  is -(CH<sub>2</sub>)<sub>n</sub>- aryl or -(CH<sub>2</sub>)<sub>n</sub> heteroaryl;

Rb is aryl or heteroaryl;

Rc is -CH2 aryl or aryl;

15

Rd is hydrogen or C1-C6 alkyl;

 $R^e$  is  $-CH_2$  aryl or  $-CH_2$  heteroaryl; and the pharmaceutically acceptable salts, esters, amides, and prodrugs thereof.

42. A compound according to Claim 41 wherein R<sup>1</sup> is

Reo O

43. A compound according to Claim 41 wherein R<sup>1</sup> is

$$\mathbb{R}^{b} \overset{O}{\underset{O}{\parallel}} \overset{\circ}{\underset{O}{\parallel}}$$
.

- 44. A compound according to Claim 41 wherein Re is -(CH<sub>2</sub>)<sub>n</sub> aryl.
- 45. A compound according to Claim 41 wherein aryl is phenyl or naphthyl.
- 10 46. A compound according to Claim 41 wherein Rb is aryl.
  - 47. A compound according to Claim 46 wherein is aryl is phenyl.
  - 48. A method of inhibiting interleukin-1 $\beta$  converting enzyme, the method comprising administering to a patient in need of inhibition of interleukin-1 $\beta$  converting enzyme a therapeutically effective amount of a compound of Claim 41.
  - 49. A method of inhibiting Caspase-4, the method comprising administering to a patient in need of Caspase-4 inhibition a Caspase-4 inhibiting amount of a compound of Claim 41.

-47-

- 50. A method of treating or preventing stroke, the method comprising administering to a patient having a stroke or having had a stroke a therapeutically effective amount of a compound of Claim 41.
- 51. A method of treating inflammatory diseases, the method comprising
  administering to a patient having an inflammatory disease a therapeutically
  effective amount of a compound of Claim 41.
  - 52. The method of Claim 51 wherein the inflammatory disease is arthritis.
  - 53. The method of Claim 51 wherein the inflammatory disease inflammatory bowel disease.
- 10 54. A method of treating septic shock, the method comprising administering to a patient having septic shock a therapeutically effective amount of a compound of Claim 41.
  - 55. A method of treating reperfusion injury, the method of comprising administering to a patient having reperfusion injury a therapeutically effective amount of a compound of Claim 41.
    - 56. A method of treating Alzheimer's disease, the method comprising administering to a patient having Alzheimer's disease a therapeutically effective amount of a compound of Claim 41.
- 57. A method of treating shigellosis, the method comprising administering to a patient having shigellosis a therapeutically effective amount of a compound of Claim 41.
  - 58. The compounds:
    - 3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-propionylamino]-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid;

10

15

20

3-[2-(2-Benzyloxycarbonylamino-4-carboxy-butyrylamino)-3-		
methyl-butyrylamino]-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoic		
acid;		
3-{2-[4-Carboxy-2-(3-phenyl-propionylamino)-butyrylamino]-3-		
methyl-butyrylamino}-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoid		
acid;		
3-[2-(2-Benzyloxycarbonylamino-3-methyl-butyrylamino)-		
propionylamino]-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-		
ylmethanesulfonylamino)-4-oxo-pentanoic acid;		
3-[2-(2-Benzyloxycarbonylamino-4-carboxy-butyrylamino)-3-		
methyl-butyrylamino]-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-		

ylmethanesulfonylamino)-4-oxo-pentanoic acid;
3-{2-[4-Carboxy-2-(3-phenyl-propionylamino)-butyrylamino]-3-methyl-butyrylamino}-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-

ylmethanesulfonylamino)-4-oxo-pentanoic acid;

3-(2-{2-[2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino]-4-carboxy-butyrylamino}-3-methyl-butyrylamino)-5-(7,7-dimethyl-2-oxo-bicyclo[2.2.1]hept-1-ylmethanesulfonylamino)-4-oxo-pentanoic acid; and

3-(2-{2-[2-Acetylamino-3-(4-hydroxy-phenyl)-propionylamino]-4-carboxy-butyrylamino}-3-methyl-butyrylamino)-4-oxo-5-(2-phenyl-ethanesulfonylamino)-pentanoic acid.